

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: DIET DRUGS (PHENTERMINE/
FENFLURAMINE/DEXFENFLURAMINE)
PRODUCTS LIABILITY LITIGATION

MDL NO. 1203

FILED

FEB -6 2014

MICHAEL KUNZ, Clerk
By _____ Dep. Clerk

THIS DOCUMENT RELATES TO:

SHEILA BROWN, et al.

v.

CIVIL ACTION NO. 99-20593

AMERICAN HOME PRODUCTS
CORPORATION

2:16 MD 1203

MEMORANDUM IN SUPPORT OF SEPARATE PRETRIAL ORDER NO. 9203

Bartle, J.

February 5, 2014

Michael Hirschbein ("Mr. Hirschbein" or "claimant") a class member under the Diet Drug Nationwide Class Action Settlement Agreement ("Settlement Agreement") with Wyeth,¹ seeks benefits from the AHP Settlement Trust ("Trust").² Based on the record developed in the show cause process, we must determine whether claimant has demonstrated a reasonable medical basis to support his claim for Matrix Compensation Benefits ("Matrix Benefits").³

1. Prior to March 11, 2002, Wyeth was known as American Home Products Corporation. In 2009, Pfizer, Inc. acquired Wyeth.

2. Sandra Hirschbein, Mr. Hirschbein's spouse, also has submitted a derivative claim for benefits.

3. Matrix Benefits are paid according to two benefit matrices (Matrix "A" and Matrix "B"), which generally classify claimants for compensation purposes based upon the severity of their

(continued...)

To seek Matrix Benefits, a claimant must first submit a completed Green Form to the Trust. The Green Form consists of three parts. The claimant or the claimant's representative completes Part I of the Green Form. Part II is completed by the claimant's attesting physician, who must answer a series of questions concerning the claimant's medical condition that correlate to the Matrix criteria set forth in the Settlement Agreement. Finally, claimant's attorney must complete Part III if claimant is represented.

In June, 2011, claimant submitted a completed Green Form to the Trust signed by his attesting physician, Manoj R. Muttreja, M.D. Based on an echocardiogram dated May 19, 2002, Dr. Muttreja attested in Part II of Mr. Hirschbein's Green Form that claimant suffered from mild aortic regurgitation and had surgery to repair or replace the aortic and/or mitral valve(s)

3. (...continued)

medical conditions, their ages when they are diagnosed, and the presence of other medical conditions that also may have caused or contributed to a claimant's valvular heart disease ("VHD"). See Settlement Agreement §§ IV.B.2.b. & IV.B.2.d.(1)-(2). Matrix A-1 describes the compensation available to Diet Drug Recipients with serious VHD who took the drugs for 61 days or longer and who did not have any of the alternative causes of VHD that made the B matrices applicable. In contrast, Matrix B-1 outlines the compensation available to Diet Drug Recipients with serious VHD who were registered as having only mild mitral regurgitation by the close of the Screening Period or who took the drugs for 60 days or less or who had factors that would make it difficult for them to prove that their VHD was caused solely by the use of these Diet Drugs.

following the use of Pondimin[®] and/or Redux[™].⁴ Based on such findings, claimant would be entitled to Matrix A-1, Level III benefits in the amount of \$760,588.⁵

In the report of claimant's November 3, 2010 echocardiogram, the reviewing cardiologist, Ashok K. Agarwal, M.D., F.A.C.C., noted "aortic stenosis" with an "aortic valve area of 0.9 cm square." Dr. Muttreja, however, attested in claimant's Green Form that Mr. Hirschbein did not suffer from aortic stenosis. Under the Settlement Agreement, the presence of aortic stenosis, which is defined as "[a]ortic stenosis with an aortic valve area < 1.0 square centimeter by the Continuity Equation," requires the payment of reduced Matrix Benefits. See Settlement Agreement § IV.B.2.d.(2)(c)i)e). As the Trust does not contest Mr. Hirschbein's entitlement to Level III benefits, the only issue before us is whether claimant is entitled to payment on Matrix A-1 or Matrix B-1.

In October, 2011, the Trust forwarded the claim for review by M. Michele Penkala, M.D., one of its auditing cardiologists. In audit, Dr. Penkala concluded that there was no reasonable medical basis for Dr. Muttreja's finding that claimant

4. Dr. Muttreja also attested that claimant suffered from a reduced ejection fraction in the range of 50% to 60%. This condition is not at issue in this claim.

5. Under the Settlement Agreement, a claimant is entitled to Level III benefits if he or she suffers from "left sided valvular heart disease requiring ... [s]urgery to repair or replace the aortic and/or mitral valve(s) following the use of Pondimin[®] and/or Redux[™]." See Settlement Agreement § IV.B.2.c.(3)(a).

did not have aortic stenosis with an aortic valve area of less than 1.0 square centimeter by the Continuity Equation. In support of this conclusion, Dr. Penkala explained:

Based on the [echocardiogram] study dated 11/3/10 the [aortic valve area] was $<0.9\text{cm}^2$ (x gradient 38 mmHg + peak 52 mmHg.) There was no [aortic valve area] mentioned on the heart [catheterization] report dated 1/5/11 but the peak to peak gradient was 40 mmHg. At the time of the [intraoperative] inspection the [aortic valve] was noted to be "a three-leaflet valve, severely stenotic."

Based on Dr. Penkala's finding, the Trust issued a post-audit determination that Mr. Hirschbein was entitled only to Matrix B-1, Level III benefits. Pursuant to the Rules for the Audit of Matrix Compensation Claims ("Audit Rules"), claimant contested this adverse determination.⁶ In contest, claimant argued that the auditing cardiologist erred by finding aortic stenosis as defined in the Settlement Agreement. In support, claimant submitted declarations from Dr. Muttreja and Paul W. Dlabal, M.D., F.A.C.P., F.A.C.C., F.A.H.A. In his declaration, Dr. Muttreja stated, in pertinent part, that:

3. In my opinion, even the 11/03/10 echocardiogram did not show an aortic valve area (AVA) less than 1.0 cm^2 , and there is a reasonable medical basis for this finding.

6. Claims placed into audit on or before December 1, 2002 are governed by the Policies and Procedures for Audit and Disposition of Matrix Compensation Claims in Audit, as approved in Pretrial Order ("PTO") No. 2457 (May 31, 2002). Claims placed into audit after December 1, 2002 are governed by the Audit Rules, as approved in PTO No. 2807 (Mar. 26, 2003). There is no dispute that the Audit Rules contained in PTO No. 2807 apply to Mr. Hirschbein's claim.

4. On the 11/03/10 echocardiogram, there was only one loop (#55) that showed any gradients using continuous wave doppler recordings. There were only three (3) full signals (beats) and a $\frac{1}{2}$ signal recorded on this loop. The overall quality of the signal recording was poor. In my opinion, one could not accurately trace the gradients given the quality and faintness of these signals.

5. On the 11/03/10 echocardiogram, the technician traced the first gradient from the first signal on loop #55. This gradient grossly appeared to be the highest gradient, and it was likely over-traced by the technician. As noted by Dr. Penkala, the peak gradient was 52 mmHG and the mean gradient was 38 mmHg.

6. In choosing a gradient for the Continuity Equation, the cardiologist should review multiple signals or beats, and he/she should choose the signal that is very similar or representative of other signals found throughout the study. By reviewing multiple signals, the cardiologist will avoid the use of an aberrant gradient, such as one that may result from a premature ventricular contraction or a premature atrial contraction that occurred before the recorded signal.

7. By using gradients only from the beats that occur regularly, the cardiologist will avoid falsely elevated gradients which will result in erroneous reports of smaller AVAs.

8. In this case, Dr. Penkala used what appeared to be the highest gradient from the first signal, without regard to whether or not the preceding beat might have created an aberrant gradient.

9. A more representative doppler signal would be either the second or third signal on loop #55. Although the gradients from these signals were not traced by the technician, these gradients clearly showed peaks and means that were less than the 52 mmHg and 38 mmHg used by Dr. Penkala. Therefore, in reasonable medical certainty, the calculated

AVA would be greater than 1.0 cm^2 when using these lower gradients.

10. The cardiac catheterization confirmed that the second and third beats (signals) were more representative of the other beats. The catheterization report did not provide an AVA calculated, but it did give a peak-to-peak gradient of 40 mmHg. The peak-to-peak gradient is similar to the peak gradient that is obtained from the echocardiogram dated 11/03/10, and these two variables should be within the same range.

11. The peak-to-peak gradient of 40 mmHg was markedly lower than the 52 mmHg which was used by Dr. Penkala. This peak-to-peak gradient was much more in line with the gradient that likely would have been obtained from the second or third beats (signals) in loop #55.

12. As set forth above, in reasonable medical certainty, the gradients obtained from the second and third beats would have yielded a calculated AVA greater than 1.0 cm^2 . In reasonable medical certainty, if all of the data from the catheterization were available, this data would also support a calculated AVA greater than 1.0 cm^2 .

In his declaration, Dr. Dlabal stated that claimant's November 3, 2010 echocardiogram demonstrated an aortic valve area of either 1.1 or 1.2 cm^2 . In addition, he explained, in pertinent part, that:

Furthermore, the maximum gradient across the aortic valve (AoV), derived from this data, equals 34 mmHg. vs 55 mmHg read by Dr. Agarwal, which I believe to be derived from an overestimation of the AoV Velocity reading above (i.e., he read AoV Velocity = 3.6 M/sec, which is not supported by careful analysis of the source data). My interpretation corresponds to the mean gradient = 38 mmHg, which was, in fact, confirmed by Dr. Agarwal.

In addition, claimant argued that Dr. Penkala improperly relied on a "totality of the medical records and documentation" approach. (Emphasis omitted). Finally, Mr. Hirschbein argued that Dr. Penkala was not qualified to serve as an auditing cardiologist.⁷

Although not required to do so, the Trust forwarded the claim to the auditing cardiologist for a second review. Dr. Penkala submitted a declaration in which she again concluded that there was no reasonable medical basis for the attesting physician's representation that Mr. Hirschbein did not have aortic stenosis. In her declaration, Dr. Penkala stated, in pertinent part, that:

9. I disagree with the conclusion of Drs. Muttreja and Dlabal, that the 11/3/10 study does not demonstrate Aortic Stenosis. As noted by Dr. Muttreja, image #55 demonstrates the [continuous wave] recordings across the [aortic valve]. Although the signal is somewhat faint, it is clearly discernable and very consistent across each of the recordings. The peak velocity by visual estimate on each signal is very consistent and the signal that the technician chose to trace has a very representative peak velocity of 3.59m/s. The gradient was not "over traced by the technician" but rather appears quite accurate. Dr. Muttreja expresses concern that this may have been an "aberrant gradient...may result from a PVC or

7. Claimant also argued that his claim should not be reduced to Matrix B-1 based on his November 3, 2010 echocardiogram because the Settlement Agreement and the Seventh Amendment dictate that a claim be reduced only when one or more of the enumerated conditions existed at the time claimant was diagnosed as FDA Positive. We have repeatedly rejected this argument. See, e.g., PTO No. 8822, at 9-12 (Feb. 22, 2012), aff'd, 525 F. App'x 140 (3d Cir. 2013).

PAC that occurred before the recorded signal." Given that I did not find any evidence of ectopy throughout the entire recording and that the signal, albeit somewhat faint, was representative of all the [Continuous Wave] signals. I do not believe that this is a legitimate concern.

10. I also recalculated the [aortic valve area] based on the continuity equation, using my own measurements for the [left ventricular outflow tract] dimension (21mm) and the peak [left ventricular outflow tract] velocity of 0.9m/s (which appears to me to be representative based on clips 50-51), and utilizing the [aortic valve] peak of 3.59m/s. With these very reasonable values I obtained an [aortic valve area] of 0.86cm^2 , which meets the Settlement Agreement criteria for [aortic stenosis].

11. While Dr. Dlabal uses different velocities in his calculations, I did not find these to be accurate. I utilized the [left ventricular outflow tract] peak velocity of 0.9 cm² from loops 50, 51 and 52 all of which appeared consistent and sampled from about 3-5mm proximal to the [aortic valve] per convention.

12. Additionally, the 2D appearance of the [aortic valve] in both the parasternal long and short axis views clearly appears very abnormal with marked calcification and thickening of the leaflets as well as marked restriction to opening. In fact it appears in the short axis view (clip 23) that only the commissure between the NCC/RCC actually opens to a reasonable degree.

The Trust then issued a final post-audit determination, again determining that Mr. Hirschbein was entitled only to Matrix B-1, Level III benefits. Claimant disputed this final determination and requested that the claim proceed to the show cause process established in the Settlement Agreement. See Settlement Agreement § VI.E.7.; PTO No. 2807, Audit Rule 18(c).

The Trust then applied to the court for issuance of an Order to show cause why Mr. Hirschbein's claim should be paid. On May 3, 2012, we issued an Order to show cause and referred the matter to the Special Master for further proceedings. See PTO No. 8866 (May 3, 2012).

Once the matter was referred to the Special Master, the Trust submitted its statement of the case and supporting documentation. Claimant then served a response upon the Special Master. The Trust submitted a reply on November 15, 2012, and claimant submitted a sur-reply on December 3, 2012. Under the Audit Rules it is within the Special Master's discretion to appoint a Technical Advisor⁸ to review claims after the Trust and claimant have had the opportunity to develop the Show Cause Record. See Audit Rule 30. The Special Master assigned a Technical Advisor, Gary J. Vigilante, M.D., F.A.C.C., to review the documents submitted by the Trust and claimant and to prepare a report for the court. The Show Cause Record and Technical Advisor Report are now before the court for final determination. See id. Rule 35.

The issue presented for resolution of this claim is whether claimant has met his burden of proving that there is a

8. A "[Technical] [A]dvisor's role is to act as a sounding board for the judge--helping the jurist to educate himself in the jargon and theory disclosed by the testimony and to think through the critical technical problems." Reilly v. United States, 863 F.2d 149, 158 (1st Cir. 1988). In a case such as this, where conflicting expert opinions exist, it is within the discretion of the court to appoint a Technical Advisor to aid it in resolving technical issues. Id.

reasonable medical basis for the attesting physician's finding that he did not have aortic stenosis with an aortic valve area of less than 1.0 square centimeter by the Continuity Equation. See id. Rule 24. Ultimately if we determine that there is no reasonable medical basis for the answer in claimant's Green Form that is at issue, we must affirm the Trust's final determination and may grant such other relief as deemed appropriate. See id. Rule 38(a). If, on the other hand, we determine that there is a reasonable medical basis for the answer, we must enter an Order directing the Trust to pay the claim in accordance with the Settlement Agreement. See id. Rule 38(b).

In support of his claim, Mr. Hirschbein reasserts many of the arguments he raised in contest. In addition, he argues that Dr. Penkala concealed evidence and relied on "outlier" measurements that were not representative to calculate his aortic valve area. In support, Mr. Hirschbein submitted a supplemental declaration of Dr. Dlabal, along with a still-frame image purporting to support his opinion.

In response, the Trust argues that the auditing cardiologist did not improperly rely on Mr. Hirschbein's cardiac catheterization study and other medical documentation because she specifically determined that claimant's November 3, 2010 echocardiogram demonstrated aortic stenosis as defined by the Settlement Agreement. In addition, the Trust contends that claimant has failed to provide a reasonable medical basis for Dr. Muttreja's representation to the contrary.

The Technical Advisor, Dr. Vigilante, reviewed claimant's echocardiogram and concluded that there was no reasonable medical basis for the attesting physician's finding that Mr. Hirschbein did not have aortic stenosis with an aortic valve area less than 1.0 square centimeter by the Continuity Equation. Specifically, Dr. Vigilante concluded:

I reviewed Claimant's echocardiogram of November 3, 2010.... This was a fair quality study with the usual echocardiographic views obtained. The Nyquist limits were appropriately set. There was appropriate evaluation of the left ventricular outflow tract velocity by pulse wave Doppler and adequate evaluation of the increased velocity across the stenotic aortic valve with continuous wave Doppler.

Evaluation of the aortic valve demonstrated that this was a heavily calcified structure with marked restriction of aortic leaflet excursion on all views including parasternal long-axis, parasternal short-axis, and apical long-axis views. In the parasternal long-axis view, the left ventricular outflow tract height was 2.0 cm.... Doppler evaluation of the aortic valve in the apical views was appropriate. Loop 55 demonstrated the peak velocity across the stenotic aortic valve. There were four cardiac cycles demonstrating the velocity. All of them showed a high velocity. The best envelope was noted in the first cardiac cycle and this was appropriately used by the sonographer for tracing the velocity time interval ("VTI"). Continuous wave Doppler evaluation in the other three cardiac cycles were the same velocity although the envelope was not as intense.

I disagree with Dr. Muttreja and Dr. Dlabal that the other velocities were lower. My independent measurements and calculations of the Continuous Wave Doppler across the aortic valve found to a peak velocity of 3.6 m/sec and a VTI of 0.85 m. Review of the pulse

wave Doppler in the left ventricular outflow tract demonstrated that this was best evaluated in loop 56 as documented by Dr. Dlabal. Indeed, this was the same image used by the sonographer for calculations of the peak velocity and the VTI in the left ventricular outflow tract. My independent evaluation of this velocity demonstrated that the peak velocity was 1.1 m/sec and the VTI was 0.25 m. Therefore, my calculation of the aortic valve area using the Continuity Equation was 0.92 cm² which is less than 1.0 cm². It should be noted that the sonographer's calculation of the VTI in the left ventricular outflow tract was 0.24 m and the calculation of the VTI through the aortic valve was 0.84 m which correspond very well to my independent measurements and calculations. Even if the less accurate peak velocities rather than velocity time integrals are used in the Continuity Equation, the calculated aortic valve area is still less than 1.0 cm². My calculations correspond well with those performed by the sonographer on this study. The sonographer used the highest representative continuous wave Doppler across the stenotic aortic valve as well as the highest representative velocity in the left ventricular outflow tract. The sonographer's calculations of the peak velocities and VTI's are very similar to my calculations. In her Declaration, Dr. Penkala appropriately used the peak velocity of 3.59 m/sec in her calculation of the aortic valve area. However, she inappropriately used a lower left ventricular outflow tract velocity of 0.9 m/sec in her calculation. The correct left ventricular outflow tract velocity was 1.1 m/sec.

Dr. Muttreja was incorrect stating that the highest gradient across the aortic valve was over-traced by the technician. The technician performed correct calculations. The signals in loop 55 showed similar velocities although the envelope is not as dense. Dr. Dlabal was incorrect using an aortic valve velocity of 2.9 m/sec from loop 55. He was incorrect in stating that the three other beats on loop 55 had much lower velocities. Indeed, these three other beats

had the same velocities as the first beat. However, I do agree with Dr. Dlabal's evaluation of the left ventricular outflow tract velocity from loop 56 and, indeed, I used this loop in the calculation of the aortic valve area using the Continuity Equation. It should be also noted that the finding of a 40 mm peak-to-peak gradient on cardiac catheterization is different than a peak gradient found on echocardiography. In addition, the echocardiographic and cardiac catheterization studies were performed at different times and under different conditions.

In response to the Technical Advisor Report, claimant argues that Dr. Vigilante substituted his own opinion for that of the attesting physician rather than apply the reasonable medical basis standard. In addition, claimant contends that the Technical Advisor did not consider Dr. Penkala's and Dr. Dlabal's left ventricular outflow tract diameter or the aortic valve velocities in loop 57, and that Dr. Vigilante did not record his findings. Finally, Mr. Hirschbein asserts that Dr. Vigilante failed to average the aortic valve velocities from a number of beats in order to obtain a representative measurement and failed to use normal clinical judgment and accepted medical standards. In particular, Mr. Hirschbein argues that Dr. Vigilante erred because he expressed his measurements to the tenth place rather than to the hundredth place.

After reviewing the entire show cause record, we find claimant has failed to meet his burden of demonstrating that he is entitled to Matrix A-1 benefits. The Settlement Agreement requires that a claim for benefits based on damage to the aortic

valve be reduced to Matrix B-1 if claimant had aortic stenosis with an aortic valve area less than 1.0 square centimeter by the Continuity Equation. See Settlement Agreement § IV.B.2.d.(2)(c)(i)e).

Here, the report of claimant's November 3, 2010 echocardiogram notes that Mr. Hirschbein had "aortic stenosis" with an "aortic valve area of 0.9 cm square." Although Dr. Muttreja and Dr. Dlabal contend that the technician who performed his November 3, 2010 echocardiogram over-traced the highest gradient, Dr. Penkala reviewed the echocardiogram and determined that "the signal that the technician chose to trace has a very representative peak velocity" She explained, "[T]he peak velocity by visual estimate on each signal is very consistent"⁹ Dr. Vigilante also concluded that "[t]he technician performed correct calculations." According to Dr. Vigilante, "The signals in loop 55 showed similar velocities although the envelope is not as dense."

Moreover, the auditing cardiologist and the Technical Advisor independently determined that claimant's aortic valve area was less than 1.0 square centimeter. Specifically, Dr. Penkala concluded that Mr. Hirschbein's aortic valve area was less than 0.9 cm². Dr. Vigilante similarly found that

9. Thus, we reject claimant's argument that Dr. Vigilante improperly concluded that the velocity was the same in three of the cycles or that he needed to average the aortic valve velocities from a number of beats to obtain a representative measurement.

Mr. Hirschbein's "aortic valve area using the Continuity Equation was 0.92 cm²" and that "[a]n echocardiographer could not reasonably conclude that the aortic valve area was greater than 1.0 cm² on [claimant's November 3, 2010] study even taking into account inter-reader variability when appropriate measurements and calculations were performed on the proper Doppler images."¹⁰

For the foregoing reasons, we conclude that claimant has not met his burden of proving that there is a reasonable medical basis for finding that he did not have aortic stenosis with an aortic valve area of less than 1.0 square centimeter by the Continuity Equation. Therefore, we will affirm the Trust's denial of Mr. Hirschbein's claim for Matrix A, Level III benefits and the related derivative claim submitted by his spouse.

10. For this reason as well, we reject claimant's assertion that Dr. Vigilante substituted his own opinion for that of the attesting physician.